REMARKS

Claims

Claims 2, 8 and 10 are currently under examination with claims 11–12 withdrawn from consideration due to restriction/election and claims 1, 3–7 and 9 cancelled without prejudice or disclaimer. Claims 13–17 are added by this paper.

Claim amendments

The claims have been amended as per conventional US practice and to correct minor typographical errors. For example, use claims have been amended to recite process claims.

New independent claim 13 is recites the elected invention (for example, "a method for the prevention or treatment of a process...") and is moreover directed to the elected species (for example, wherein the compound acts on a growth factor receptor ligand precursor). Support for the claim can be found in, for example, page 3, lines 20–21 and page 4, lines 16–20 of the originally-filed specification. Previously presented claims 2, 8, and 10, along with newly presented claims 14–16 are either directly or indirectly dependent on independent claim 13. Search and examination of the instantly presented claims is earnestly solicited.

New claims 14–16 are supported, at least, by the disclosure contained in page 3, lines 4–21 of the originally-filed specification.

It is respectfully submitted that the claim amendments do not raise new matter.

IDS

Copies of non-patent literature publications are enclosed herewith, rendering the objection thereof moot.

Specification

The specification has been amended to establish the chain of priority.

The specification has been amended to include a Brief Description of the Drawings section, the support for which can be found in the disclosure contained in the Examples and the respective title/content of the Figures. It is respectfully submitted that the amendment does not raise new matter.

The allegation that the "figure legends...do not describe in brief but sufficient detail the data contained in any of the figures" is respectfully traversed. Inasmuch as descriptive portion of

the specification and the Examples clearly describe the data contained in the Figures and the Tables, explicit description thereof is not necessary. For example, the skilled artisan can readily ascertain that Fig. 1 relates to an immuno-blotting experiment.

The ABSTRACT has been moved from the cover-page of the published PCT application to the end of the specification, in conformance with the USPTO rules.

The specification has been amended to incorporate Table 1, which is now cancelled from the drawings.

Applicants thank the Examiner for her suggestion with respect to the arrangement of the specification. However, the objection is respectfully traversed insofar as the descriptive portion of Applicants' specification and the experimental section allow one of ordinary skill in the art to practice the claimed invention in its broadest possible scope. Absolute adherence to such (for example, dividing the specification using specific headers) is not necessary. See, MPEP §608.01.

Withdrawal of the objection is respectfully requested.

Rejections under §101 and 112, ¶2

The foregoing amendments render the examiner's comments in paragraphs 8-10 moot.

Rejections under 35 U.S.C. §102

The contention that the instantly claimed subject matter is anticipated by Prenzel (*Nature*, 1999), Freeman (*J. Cellular Biochemistry*, 1998), Wallasch (WO 01/35899) Hanke (WO 00/77195), Ito (*BBC*, 1996) or Elder (US publication No. 2002/0169176; filed: February 11, 2002 and claims priority to US provisional No. 60/268,220) is respectfully traversed.

At the outset, it is submitted that the rejection is moot in view of the amendments. However, the following arguments are provided in favor of the novelty of claimed invention over the disclosure(s) contained in the cited art references.

Prenzel describes the effects of diphtheria toxin CRM197, a non-toxic mutant of diphtheria toxin, on phosphorylation of EGFR. See, col. 1, ¶3–4 at page 886 of Prenzel. The reference is silent as to an antibody which binds to pro-HB-EGF.

Freeman describes a specific anti HB-EGF antibody, which binds to the domain of pro-HB-EGF bound to the membrane. See, the paragraph bridging col. 1 and col. 2 at page 331 of Freeman. However, the reference is silent with respect to the growth-inhibitory effects of this antibody molecule and/or use thereof in a manner recited in Applicants' claims.

Wallasch is drawn to the use of inhibitors of membrane-associated metal proteinases in the treatment of diseases caused by *Helicobacter pylori*. The reference is silent with respect to an antibody molecule and/or properties thereof in a manner recited in the present claims.

Hanke relates to nucleic acid molecules which encode an EGFR ligand. The reference is silent with respect to pro-HB-EGF and/or antibodies thereto. Since not all material elements of the present claims are disclosed in Hanke et al., the cited reference cannot anticipate what is claimed by the present invention.

The ABSTRACT by Ito teaches the use of an anti-HB-EGF antibody which inhibits DNA synthesis in EP170.7 cells. The reference fails to teach or suggest *any* pro-HB-EGF molecules including properties thereof. There is also no mention of antibody molecules that bind to pro-HB-EGF and use of such molecules in a manner recited in Applicants' claims.

Elder discloses use of a composition comprising Erb inhibitor(s) and retinoid(s) for the treatment of skin diseases and injuries thereto. In col. 15, ¶335 of the publication, Elder discloses a polyclonal antibody against HB-EGF. There is no mention of a pro-HB-EGF antibody in Elder. Furthermore, the reference is silent as to the use of such antibody molecules in a manner recited in present claims. See, independent claim 13.

As such, it is respectfully submitted that none of the aforementioned teachings anticipates the subject matter of the present claims. For anticipation, the references have to teach each and every element recited in Applicants' claims. Withdrawal of the rejection is respectfully requested.

Rejection under §112, ¶1

The contention that the subject matter of the present claims is non-enabled is respectfully traversed.

Applicants' instant specification coupled with a skilled worker's knowledge provides adequate guidance to use the claimed molecules (for example, an antibody which binds to pro-HB-EGF) for the methods claimed herein. The specification provides both general and specific guidance regarding the relationship between the activity of pro-HB-EGF molecules with respect to the specific processes recited in the claims, for example, cell proliferation, cell migration, invasivity and/or anti-apoptosis. See, for example, the disclosure contained in the paragraph bridging pages 2 and 3 and page 3, lines 8–21 of the instant specification. Applicants' specification, for example, page 4, lines 18–20 expressly teaches that the claimed invention relates to treatment or prevention of cancer such as that of colon, kidney, liver, bladder, pancreas,

prostate, GI, breast, lung, thyroid, pituitary, adrenal, ovarian or glial tissue. This is further corroborated by the experimental evidence provided in the Examples.

Using antibody molecules which bind to pro-HB-EGF as a representative example, the specification provides more than adequate guidance for the use of the claimed molecules in a manner that is described in the claims. Furthermore, the specification in view of the references cited therein conveys to one of ordinary skill in the art that pro-HB-EGF mediates tumorigenic effects both *in vitro* as well as *in vivo*. Applicants' specification teaches a number of ways via which such tumorigenic effects may be inhibited in the clinical setting. To this end, it is expressly taught that antibody-mediated binding and sequestration of pro-HB-EGF molecules neutralizes the effect thereof *in vivo*.

In light of this detailed disclosure, the courts have placed the burden on the PTO to show otherwise. It is courteously submitted that the Examiner has not presented any evidence to refute the findings or the conclusions made in the specification or the supporting publications. In addition, no evidence has been presented to support the contention that the claimed molecules could not be used, in a manner that is commensurate with Applicants' claimed invention. Only unsupported allegations and conclusions regarding the "complexity" and "unpredictability" of the "state of the art" are provided to support the contention. There are especially weak in the face of the showing that the scientific knowledge pertaining to the use of antibody molecules that bind to growth factor receptor ligands (for example, EGF, PDGF, Her2, etc.) was mature prior to the filing date of the instant application. To this end, the Examiner is cordially requested to review the disclosure contained in enclosed US patent No.: 6,214,344 (filed April 10, 2001) which describes antibodies against hepatocyte growth factors (HGF) and use thereof in the treatment of cancer. See, the disclosure contained in Fig. 1 and 4 of Schwall et al. ('344 patent).

As such, it is respectfully submitted that within the current state of the art at the time of filing there is no basis for a rejection for lack of enablement in a case where Applicants provide more than sufficient guidance as to how the molecules can be made and their activity tested. Favorable reconsideration is respectfully requested.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

/Anthony J. Zelano/

Anthony J. Zelano, Reg. No. 27,969
Attorney/Agent for Applicant(s)

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

Attorney Docket No.: WEICKM-0041

Date: April 9, 2008

Encl.
(a) Non-patent literature references